Case Report

Tumefactive Multiple Sclerosis: diagnostic study considering the differential diagnosis from other brain lesions.

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ABSTRACT: Tumefactive Multiple Sclerosis (MS) is characterized by the presence of at least one lesion ≥ 2cm in diameter, with co-existing mass effect or edema. In our study, we review the advanced Magnetic Resonance Imaging (MRI) techniques used in the diagnosis of tumefactive MS, as well as the spectrum of differential diagnosis from other brain tumors. We also present two cases of tumefactive MS. In conclusion, tumefactive MS should always be part of the differential diagnosis in each patient with radiological features of tumor-like brain lesions, in order to avoid unnecessary interventional diagnostic procedures.

Key Words: Tumefactive lesions, Multiple sclerosis, MRI techniques.

INTRODUCTION

Multiple sclerosis is an inflammatory demyelinating disorder of CNS, that may appear with a variety of different clinical presentations and laboratory findings. Tumefactive MS is a type of MS which is characterized by the presence of at least one lesion ≥ 2cm in diameter[1]. Radiologically, it presents as single or multiple contrast-enhanced lesions, with co-existing mass effect and edema ≥ 3mm. The presence of cystic or necrotic areas is also possible[2].

The contribution of modern MRI techniques in the diagnosis and differential diagnosis of tumefactive MS is strongly supported by the scientific world.

CASE REPORTS

Case 1: A 17-year-old male was referred to AHEPA hospital emergency department, with left hemiparesis and dysarthria. Two similar transitory episodes were also revealed in his medical history. Cerebrospinal fluid analysis revealed IgG oligoclonal bands, therefore indicating possible MS. The MRI showed a mass in the right semi-oval center with mediocre edema (Figure 1a). The patient had a rapid response to the conservative treatment with high doses of steroids, which was confirmed by the radiological retest (Figure 1b). Two years later, he was admitted again in the ER, with status epilepticus, right hemiparesis and walk disorders. The Computed Tomography (CT) scan only revealed the first lesion in the right hemisphere (Figure 1c). The MRI confirmed a second tumefactive lesion in the opposite hemisphere, with spotted enhancement, while the first lesion showed no enhancement (Figure 1d). The patient fully recovered after treatment with steroids.

Case 2: A 65-year-old female was admitted to our hospital with acute right hemianopsia. The CT carried out a few hours afterwards (Figure 2a) , as well as the MRI carried out a few days later, showed a left temporal-occipital mass in the cerebral parenchyma with non-homogeneous, peripheral, annular enhancement (open ring sign) and mediocre circumcentral edema. However, because of the negative laboratory examinations and the advanced age of the patient, an intracranial mass was thought to be the possible diagnosis. As a result, the mass was surgically removed (Figure 2c). However, the histological examination showed perivascular infiltration by histiocells and demyelination. Two years later, the patient was admitted with

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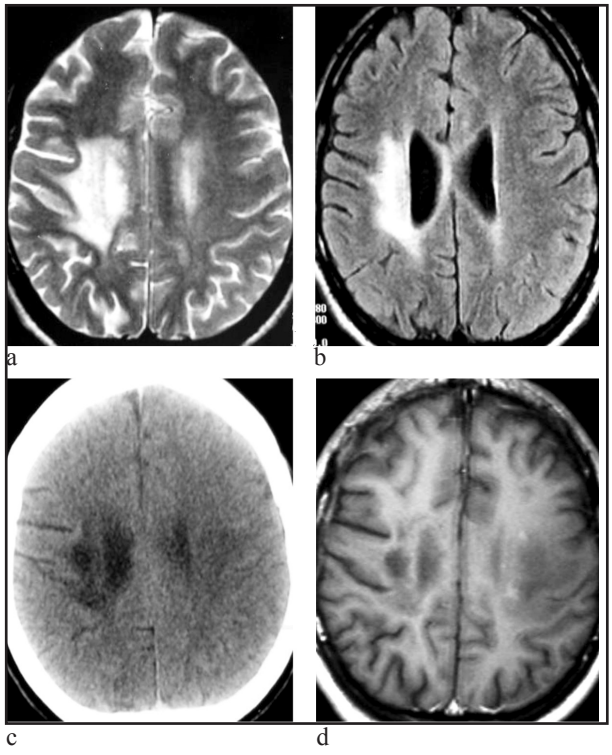

Figure 1. a. Axial T2-weighted image revealed a mass in the right semioval centre with mediocre edema. b. Axial T1-weighted image showed important restriction of the damage. c. Axial CT image showed hypointense lesion left respectively with the first lesion d.The MRI confirmed a second tumefactive lesion in opposite hemisphere, which showed spotted enhancement, while the first lesion did not show any enhancement.

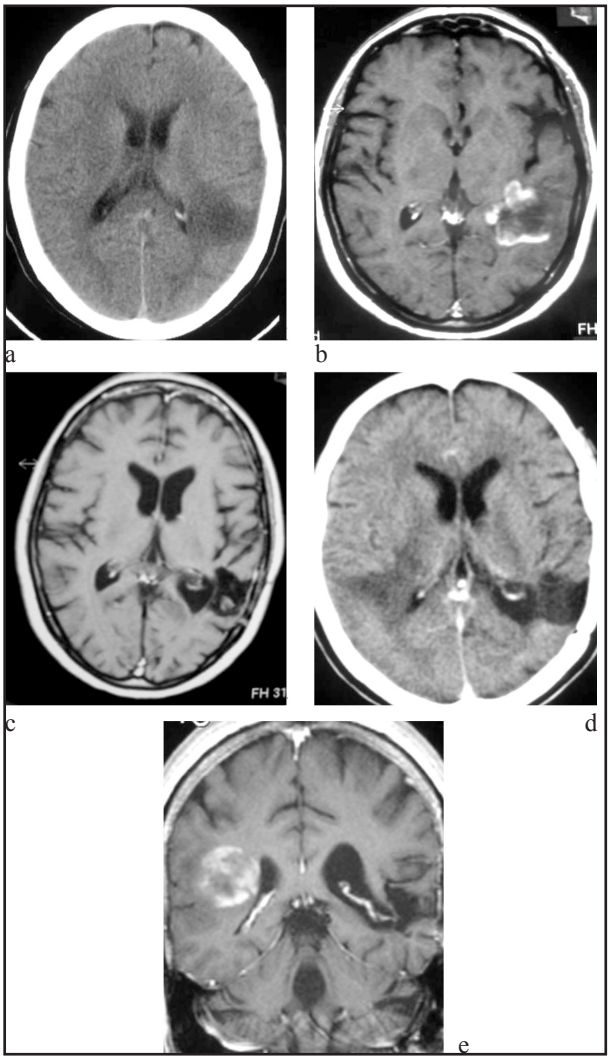

Figure 2. a. Axial CT image revealed a hypodense left temporal-occipital mass in the cerebral parenchyma. b. Axial contrast-enhanced T1- weighted image revealed a left temporal-occipital mass in the cerebral parenchyma with non-homogeneous, peripheral annular enhancement (open ring sign). c. Axial contrastenhanced T1- weighted image after the surgical removal of the mass where appears the craniotomy and the gliosis of brain respectively. d, e. Axial CT image and coronal contrastenhanced T1- weighted image revealed a second mass in opposite hemisphere with the same characteristics (open ring sign) of the first lesion.

left hemianopsia. The CT and the MRI (Figure 2d, e) showed a second mass in the opposite hemisphere with the same characteristics (open ring sign) as the first lesion. The findings of MR spectroscopy (Figure 3) spoke in favor of MS; therefore the patient was treated conservatively with steroids and showed satisfactory clinical improvement, as well as restriction of pathological enhancement in the retest (Figure 4).

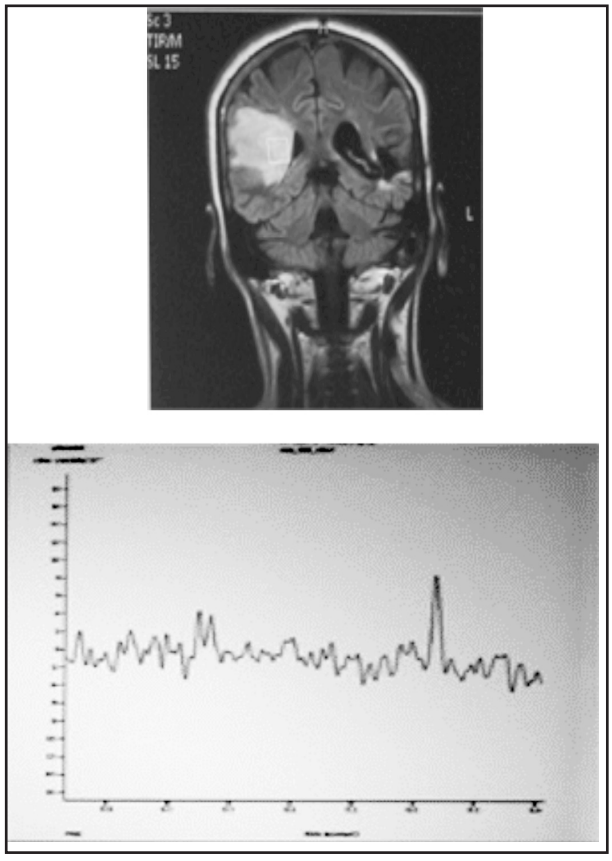

Figure 3. MR Spectroscopy of the patient which confirmed the diagnosis.

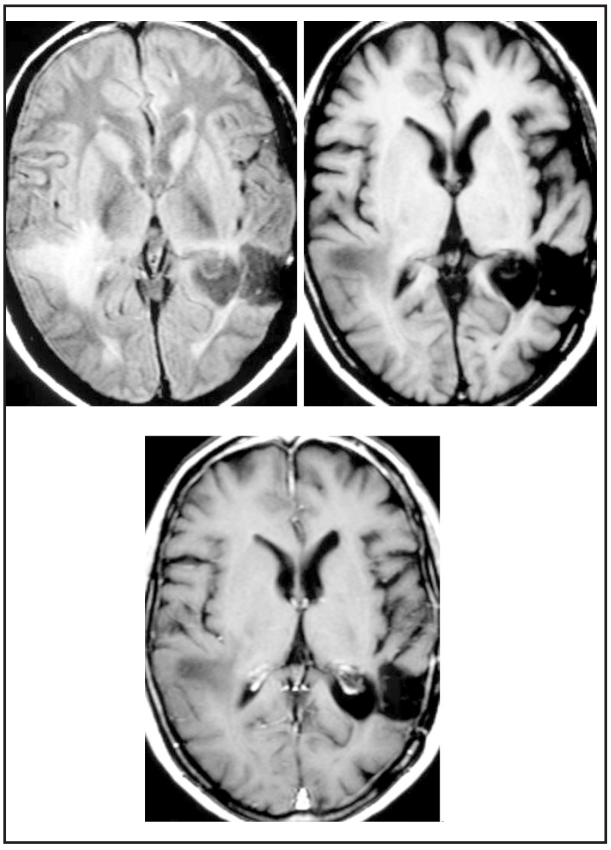

Figure 4. Axial MRI images showed restriction of pathological enhancement of lesion after dispensation of steroids.

DISCUSSION

Advanced MRI techniques have been established for better neuroimmaging evaluation in MS. In the magnetization transfer (MTR), which is related to the phenomenon of transport of magnetization, demyelination represents a progressive reduction of ratio from the periphery to the centre of the lesion[3-5]. In diffusion MRI, MS lesions appear with increased Apparent Diffusion Coeficient (ADC) reception, in contrast to cerebral abscess where reduction of ADC is observed[3]. In perfusion MRI, MS lesions show neither increase nor decrease of rCBF, in contrast to cerebral tumors where increase of rCBF is observed[3,6]. In MR spectroscopy, a reduction of NAA, Cr, β, γ-Glx and detection of LAC, CHO and lipids during the acute phase of MS, have been reported. On the contrary, during the chronic phase of MS there is an increase of NAA, Cr and disappearance of LAC and lipids[3,5,7-9]. In our study, MR spectroscopy based on measurements of metabolites β and γ-Glx was proven helpful in the differential diagnosis of MS[9]. Indeed, these markers increase in case of tumefactive MS, but not in aggressive intracranial masses (Figure 5).

Three major observations were evident in our study. The first was related to the peripheral, non-homogenous, annular enhancement of lesion, characterized as "open ring sign", which is observed in tumefactive MS[10]. The enhancement is related to blood brain barrier breakdown. Nevertheless, experimental data also report enhancement of the lesion even with intact blood brain barrier due to macrophage infiltration[2]. The second observation concerns the histopathological findings; reactive astrocytosis with atypical mitotic characteristics, foamy macrophages (myelin breakdown products) and chronic perivascular cellular infiltration cause major difficulties in differential

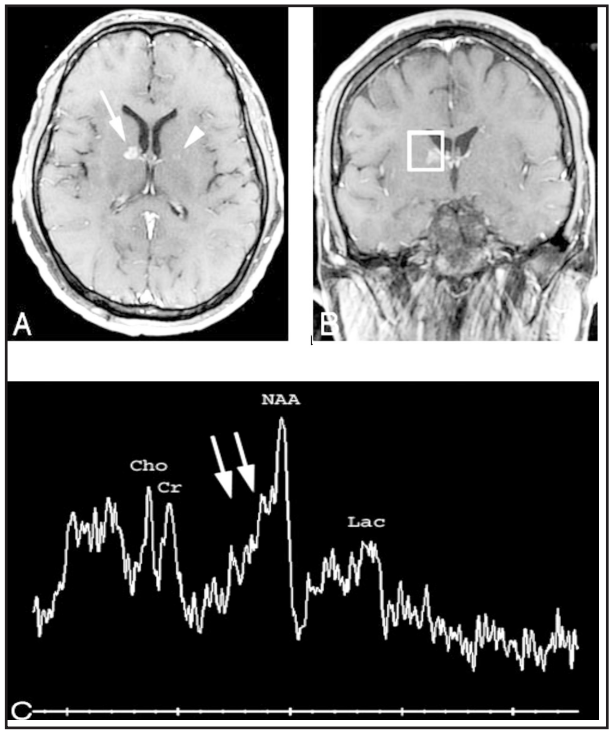

Figure 5. a. Axial T1-weighted post-contrast MR image shows a small ring-enhancing lesion in the genu of the right internal capsule (arrow) and a barely perceptible lesion in the left globus pallidus (arrowhead). Multiple additional similar small ring-enhancing lesions were identified throughout the brain parenchyma. b. Voxel localization for proton MR spectroscopy of the right internal capsule lesion. c. MR spectroscopy of the right internal capsule lesion demonstrates marked elevation of the β,γ-Glx peaks (double arrows) compared with creatine (peak height ratio 1.1 [normal less than 0.5]) compatible with tumefactive multiple sclerosis. There is also mild decrease of N-acetylaspartate and probable mild presence of lactate.

diagnosis from glioma[11]. The third observation concerns the progress of the underlying pathology and the correspondent clinical impact. Evidently despite the radiological features of the lesion, and the possibility of malignancy, it would be preferable to perform an intensive follow up with neuroimmaging for the safety of the final diagnosis rather than proceeding with the treatment such as operation or irradiation of the lesion. In addition, in case of demyelinating disorders the response to steroid therapy is usually satisfactory.

The inflammatory demyelinating brain disorders often imitate intracranial masses. The tumefactive MS should be mainly differentiated from tumors as glioma, astrocytoma and lymphoma, from other inflammatory demyelinating disorders as acute disseminated encephalomyelitis (ADEM) and from cerebral abscesses[11,12]. Certain laboratory findings, coexisting lesions in neuroradiology examinations (eg. cervical spinal cord) and rapid response to cortisone favor tumefactive MS. In the cases presented here, the distinct clinical and radiological presentations of the same disease in two different individuals, were identified. The first patient was successfully treated conservatively, on the contrary to the second one who underwent unnecessary surgical operation. In the second case the correct diagnosis was made later with the contribution of MR spectroscopy and the patient was then treated appropriately. The intracranial masses constitute an important medical problem. The role of modern imaging should not only be limited in anatomic details. The advanced MRI techniques allow us to investigate brain function; perfusion MRI gives important information about blood cerebral flow (rCBF); MR spectroscopy helps us measure various brain metabolites.

CONCLUSION

In the differential diagnosis of tumefactive brain lesions, the tumefactive MS should always be considered. Moreover, the advanced imaging techniques promise precise diagnostic approach, in order to avoid unnecessary interventional procedures for the final diagnosis and differential diagnosis.

Abbreviations:
ADC: Apparent Diffusion Coeficient
ADEM: acute disseminated encephalomyelitis
CHO: choline
Cr: creatine
LAC: lactate
MRI: Magnetic Resonance Imaging
MS: multiple sclerosis
MTR: magnetization transfer
NAA: N-acetylaspartate
rCBF: blood cerebral flow
β, γ-Glx: glutamate/glutamine

Ογκόμορφη πολλαπλή σκλήρυνση (MS): διαγνωστική μελέτη στο πλαίσιο διαφορικής διάγνωσης άλλων χωροκατακτητικών εξεργασιών του εγκεφάλου.

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ΠΕΡΙΛΗΨΗ: Ως ογκόμορφη ορίζεται η πολλαπλή σκλήρυνση που χαρακτηρίζεται από την παρουσία μίας τουλάχιστον βλάβης, διαμέτρου ≥ 2 εκ., με συνοδό φαινόμενο μάζας ή οίδημα οποιουδήποτε βαθμού. Στην εργασία γίνεται εκτενής βιβλιογραφική ανασκόπηση στις νεότερες MRI τεχνικές με τις οποίες μελετάται η ογκόμορφη πολλαπλή σκλήρυνση και τίθεται η διάγνωσή της. Αναφέρεται, ακόμη, το εύρος της διαφορικής διάγνωσης της πάθησης από άλλες χωροκατακτικές εξεργασίες του εγκεφάλου. Παρουσιάζονται, επίσης, δύο περιστατικά ασθενών με ογκόμορφη πολλαπλή σκλήρυνση. Συμπερασματικά, καταλήγουμε στο γεγονός ότι πρέπει πάντα να διερευνάται η περίπτωση της ογκόμορφης πολλαπλής σκλήρυνσης σε κάθε ασθενή με απεικονιστικά ευρήματα χωροκατακτικής μάζας του εγκεφάλου ώστε να αποφεύγονται άσκοπες επεμβατικές μέθοδοι για την τελική διάγνωση και διαφοροδιάγνωση.

Λέξεις Κλειδιά: Ογκόμορφες βλάβες, Πολλαπλή σκλήρυνση, MRI τεχνικές.

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